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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/056,230	01/24/2002	Jan E. Schnitzer	1440.1069-013	6912

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EXAMINER	
UNGAR, SUSAN NMN	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 02/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/056,230	SCHNITZER, JAN E.	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *10 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *2-17* is/are pending in the application.

4a) Of the above claim(s) *2, 6, 10-11. 15-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *3-5, 7-9, 12-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08). Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. The Amendment filed December 10, 2003 in response to the Office Action of August 8, 2003 is acknowledged and has been entered. Claims 3-5, 7-9, 12-14 are currently being examined.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The following rejections are maintained:

Claim Rejections - 35 USC § 112

4. Claims 3-5, 7-9, 12-14 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in the Paper mailed August 8, 2003, Section 6, pages 4-9.

Applicant argues that (a) Mab 833 is tissue specific to lung endothelium and to lung caveolae in particular and the data drawn to the drug dgRA with the antibody was presented as a demonstration that the antibody is capable of specifically delivering a drug to a particular tissue, (b) the broadest claims are not drawn to targeting a tumor specifically and applicant has clearly demonstrated identification and use of an antibody to deliver an agent into and across a luminal surface of vascular endothelium in a tissue-specific manner for lung tissue, (c) the methods need not be limited to treatment of malignancies and the methods claimed could be used to deliver agents for treatment of other diseases of the lung for example asthma, emphysema, tuberculosis, pneumonia, COPH, pulmonary hypertension, cystic fibrosis and other acquired or genetic lung related conditions, (d) one of ordinary skill, given the teachings of the specification regarding Mab833

would be able to identify agents that could be similarly delivered for the treatment of a wide variety of conditions.

The arguments have been considered but have not been found persuasive because (a') although Examiner agrees that Mab 833 is tissue specific to rat lung endothelium and to rat lung caveolae in particular, the issue raised was not drawn to tissue specificity, but rather was drawn to how to use the antibody Mab 833 because, although specific to rat lung and rat lung caveolae, the antibody is not specific to any disease cell type. Although the specification contemplates and claims the use of the broadly claimed "agent of interest"/antibody for therapeutic and diagnostic purposes, given only the exemplified Mab 833 which appears to be not specific for any therapeutic or diagnostic purpose, it is clear that the specification does not teach how to use the claimed invention for the contemplated and claimed function. In particular, the specification contemplates and claims the use of the antibodies taught for therapy as immunotoxins to be delivered to a tumor or other malignancy for cancer therapy (p. 16) and envisions targeting of tumor blood vessels in directed therapy, by direct delivery of an agent that targets the tumor endothelium for selective destruction while avoiding bystander noncancerous tissues (p. 17). It is clear from the drug dgRA example that the effects of targeting the rat lung with Mab 833 are non-specific within lung. There is no teaching of how to direct the broadly claimed "agent of interest" for any therapeutic or diagnostic purpose, (b') although the broadest claims are indeed not drawn to targeting a tumor specifically and applicant has clearly demonstrated identification and use of an antibody to deliver an agent into and across a luminal surface of vascular endothelium in a tissue-

specific manner for lung tissue, applicant has not taught how to use this invention. The broadly claimed invention reads on tumor specific treatment and for the reasons of record, this use is not enabled. Further, Applicant has not taught any use for the delivery of an agent into and across a luminal surface of vascular endothelium other than for therapy or diagnosis and for the reasons of record, the claims are not enabled, (c') Applicant is arguing limitations neither recited in the claims nor contemplated or taught in the specification as originally filed. Further, for the reasons of record, the specification does not teach how to specifically target the broadly claimed "agent of interest" to any cells involved in any of these diseases states or conditions, (d') contrary to Applicant's arguments, given the information in the specification one of ordinary skill in the art would know that Mab 833 could **not** be used to target any specific disease or disorder because it clearly targets caveolae on all normal lung cells. The arguments have been considered and have not been found persuasive and the rejection is maintained.

5. Claims 3-5, 7-9, 12-14 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in the Paper mailed August 8, 2003, Section 7, pages 9-13.

Applicant argues that (a) the identification of Mab 833 is not an unexpected event and the specification teaches conventional methods for identifying other tissue specific antibodies and one would understand that the important characteristic of an antibody for use in the methods is that it binds to and localizes to a component of caveolae of the luminal surface of the vascular endothelium upon contact with the luminal surface and the specification details how to test antibodies for such

specificity. The amount of experimentation is not undue, (b) one could utilize lung tissue samples from other species and easily determine whether Mab 833 functions similarly in other species and one of skill in the art could use the teachings of the specification to make and identify antibodies having similar tissue specificity in other species, (c) Mab833 can be used to isolate the rat protein to which homologues can be quickly identified in genomic databases and yield equivalent proteins for antibody generation and experimentation to do this is not undue.

The arguments have been considered but have not been found persuasive because (a') Applicant is arguing limitations not recited in the claims as currently constituted, the "agent of interest" is not limited to antibodies in claims 3-5, 8-9, 14. Further, as previously set forth, Applicant has clearly disclosed the unpredictability of the art wherein out of twenty clones tested only Mab833 was found to bind to caveolae in a lung specific fashion and as previously set forth, the specification clearly teaches the unpredictability of the art on pages 51 and 52 wherein in 20 years of research by the combined efforts of those skilled in the art, this type of effective specificity had not been previously attained. Thus for the reasons of record, the identification of Mab 833's lung caveolae specificity is an unexpected event, (b')(c') it appears that Applicant is inviting the artisan to elaborate a functional use for Mab 833 in species other than rat and it appears that Applicant has suggested that the broadly claimed invention has not been reduced to practice. Given the teachings on page 51 and 52 and add to that Applicant's suggested protocols, it is clear that undue experimentation is required to practice the claimed

invention. The argument has been considered but has not been found persuasive and the rejection is maintained.

6. Claims 3-5, 7-9, 12-14 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in the Paper mailed August 8, 2003, Section 8, pages 13-16.

Applicant argues that the specification provides a significant amount of description regarding the making and identification of a representative agent of interest and given these teachings, one would be able to identify similar agents and neither the actual antigen nor the structure of the antigen need be described provided that the antibody have the relevant characteristic, that is binding to a component of caveolae of the luminal surface of the vascular endothelium in a tissue-specific manner. Given the screening techniques, one could determine if an identified molecule functions as claimed.

The argument has been considered but have not been found persuasive because Applicant is arguing limitations not recited in claims 3-5, 8-9, 14 and contrary to Applicant's argument, description by function is not sufficient to provide written description for a claimed invention. The court has stated, in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Applying the same logic to the instantly claimed invention, other than Mab 833, the critical "agent of interest"/antibody is defined only by function and therefore the specification does not provide sufficient written description of the claimed invention.

The argument has been considered but has not been found persuasive and the rejection is maintained.

7. No claims allowed.

8. All other objections and rejections recited in the Paper mailed August 8, 2003 are hereby withdrawn.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (703) 305-2181. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvette Eyler, can be reached at 571-272-0871 The fax phone number for this Art Unit is (703) 305-7230.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.

Susan Ungar
Primary Patent Examiner
February 24, 2004